

RESPONSE TO OFFICE ACTION DATED 24 JUNE 2009

1. Rejection under 35 U.S.C. §103(a)

Claims 1–6 and 8–13 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over D’Angelo & Schur (U.S. Patent No. 5,932,240, herein “D’Angelo”) in view of Lauterbach *et al.* (U.S. Patent Application Publication No. 2003/0027793, herein “Lauterbach”).

No admission is made herein that Lauterbach (mis-spelled “Lauterback” in the published application) constitutes prior art to the present invention. Although the Examiner notes that Lauterbach has an earlier effective U.S. filing date for 102(e) purposes (12 March 2002) than the present application, it is noted that Lauterbach is not statutory prior art against the present invention, having published after the priority date of the present application. Applicant reserves the right to disqualify this publication as prior art; however, the question is moot. As shown below, even if Lauterbach were available as prior art, a *prima facie* case of obviousness has not been established over D’Angelo in view of Lauterbach.

The present Office Action maintains that it would have allegedly been obvious to a person of skill in the art “to add rotigotine free base to the transdermal delivery system . . . because D’Angelo suggest that drugs used to treat Parkinson’s disease may be included in the microreservoirs of the transdermal patch” (Action, p. 8, lines 10-13). This rejection is respectfully traversed.

1.1 Not all claim limitations are taught or suggested in the cited art

All claim limitations must be considered in judging the patentability of a claim against the prior art. MPEP 2143.03. The Office Action maintains: “In view of the fact that the cited art teaches all the instant claimed limitations, the transdermal drug delivery system encompassed by the prior art is capable of performing the intended function...” (Office Action, passage bridging p. 8-9, emphasis added) However, Applicant has previously drawn to the Examiner’s attention at least two essential elements of the present claims, namely (a) microreservoirs within a self-adhesive matrix and/or (b) microreservoirs having a maximum

diameter that is less than the thickness of the layer wherein they are embedded which are not taught or suggested in the cited art. Applicant maintains all arguments submitted in Applicant's response dated 9 March 2009.

Claim 1 recites: A transdermal delivery system (TDS) comprising a backing layer, a self-adhesive matrix containing rotigotine and a protective foil or sheet to be removed prior to use, wherein the self-adhesive matrix comprises a solid or semi-solid semi-permeable polymer

- (1) wherein rotigotine in its free base form is incorporated,
- (2) which comprises a multitude of microreservoirs within the matrix, said microreservoirs containing rotigotine,
- (3) which is permeable to the free base of rotigotine,
- (4) which is substantially impermeable to the protonated form of rotigotine, and
- (5) wherein the microreservoirs have a maximum diameter that is less than the thickness of the matrix;

and wherein the backing layer is inert to the components of the matrix.

1.1.A No teaching or suggestion of microreservoirs within a self-adhesive matrix

First, regarding microreservoirs within a self-adhesive matrix, the Office Action cites col. 7, lines 1-7 of D'Angelo and states the following:

"...it is noted that D'Angelo teach reservoirs of drug hydrogel through major openings in the layer to be applied to the skin, wherein the openings are covered with a Cotran 9710 acrylate adhesive...and therefore the Cotran 9710 acrylate adhesive defines the matrix containing the drug. Since the Coltran 9719 acrylate adhesive (= self-adhesive) is intended to be in contact with the skin and it is part of the matrix containing the drug, the matrix is necessarily self-adhesive." (Office Action, p. 10, emphasis added)

Applicant responds as follows:

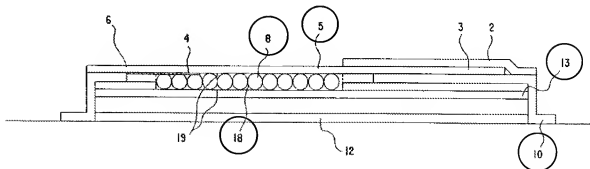
1. D'Angelo at Col. 4, lines 56-60 states: "The unit dose reservoirs of the assembly may be impressed or molded into the polymeric and impregnated materials or they may be formed by sealing the peripheries of impervious material layers to form pouches which, upon loading through openings, will become drug reservoirs." (emphasis added) These "pouches" or

“medicament/drug reservoirs” are filled with unit doses of the drug hydrogel. These should not be confused with the “microreservoirs” of the present invention which are particulate, spatially and functionally separate compartments having pure drug or a mixture of drugs within, which are small enough such that the microreservoirs of the present invention can be dispersed within a self-adhesive matrix.

2. The acrylate adhesive border 10 of D'Angelo does not equal a self-adhesive matrix containing microreservoirs of the present invention.

These are not one and the same.

- a. As noted in the Office Action above, D'Angelo states that the drug hydrogel is in "major openings in the layer to be applied to the skin". According to D'Angelo, these "openings" are covered with Cotran® 9710, a micro-porous polyethylene. This is not an acrylate adhesive. In the same paragraph, D'Angelo states: "The patch was adhered to the shaved skin by the 3M Cotran® 9872 acrylate adhesives..."(emphasis added). The D'Angelo "pouches" or "medicament/drug reservoirs" are not within the acrylate adhesive border of D'Angelo.
- b. As can be seen from D'Angelo Fig. 2 below, the hydrogel matrix 18 and microencapsulated medicament 8 of D'Angelo are sandwiched between the tear strip 5 and the permeable membrane 13. The adhesive border 10 is the outer border of the assembly for attaching the assembly to skin.



Thus, D'Angelo provides separate adhesive and drug portions of the assembly, and therefore does not disclose microreservoirs within a self-adhesive matrix as defined by the

instant invention.

1.1.B No teaching or suggestion of microreservoirs having a maximum diameter that is less than the thickness of the layer wherein they are embedded

Second, regarding microreservoirs having a maximum diameter that is less than the thickness of the layer wherein they are embedded, the Office Action states the following:

“...D’Angelo et al. teach microreservoirs having comprising [*sic*] microencapsulations of the drug active having a diameter substantially of 1 to 150 microns, wherein the microencapsulations are formed of a layer having drug-penetration moieties engrafted thereon (col. 3, lines 51-57) such that one would reasonably expect that said microreservoirs would have a maximum diameter that is less than the thickness of the self-adhesive matrix since the self-adhesive matrix provides a means to activate the reservoirs by either a “tear-and-release” or “pull and release” mechanism....Thus applicant’s argument that Lauterbach teaches away from reducing the size of the microreservoirs relative to the thickness of the patch is not found to be persuasive.” (Office Action, p. 10, emphasis added)

Applicant responds as follows:

1. Similar to the argument above, the “microencapsulations” of the drug active (*i.e.* the insulin encapsulated capsules of 1 to 150 microns diameter) are not the same as the microreservoirs of the present invention.
2. Even if the D’Angelo “microencapsulations” were the same as the microreservoirs of the present invention, the above statement contains a *non sequitor*. Why would one reasonably expect that “microreservoirs” in D’Angelo would have a maximum diameter less than the thickness of the self-adhesive matrix since the self-adhesive matrix provides a means to activate the reservoirs by a tear-and release mechanism? This goes against D’Angelo as the matrix 18 in D’Angelo is bounded by the tear strip 5 and the permeable membrane 13. There is no “self-adhesive matrix” in D’Angelo. The only adhesive in D’Angelo is at the acrylate adhesive border 10, which is used to adhere the D’Angelo patch to the skin.
3. Unlike the present invention, the D’Angelo microencapsulated medicament 8 therefore necessarily span the matrix 18 as they are attached to each of the tear strip 5 and the permeable membrane 13 by microcapsule adhesive 19. Activation of the unit dose includes pulling back the tear strip 5 so that the frangible

medicament capsules are ruptured to release medicament which diffuses through the permeable membrane 13. If the microencapsulated medicament “spans the matrix”, their diameter must be at least equal to the thickness of the matrix – whether the microcapsules are 1 micron or 150 microns.

Thus, contrary to the Office Action’s assertion, one of ordinary skill would be de-motivated by the teaching of D’Angelo because (1) D’Angelo requires its microencapsulated medicament to be “adhered to [not less than] the bottom of a tear strip 5 and to the top of a permeable membrane 13 (col. 8, lines 3–6), and (2) D’Angelo emphasizes a means for disrupting the microcapsules, which in some embodiments is achieved by pulling back the tear strip, to which the “frangible” microcapsules are adhered (col. 8, lines 34–39). One of ordinary skill would be de-motivated, by the teaching of D’Angelo regarding the significance of the disruption mechanism, to reduce the diameter of the microcapsules, such that the microcapsules no longer contact the layers above and below the matrix in which they are embedded.

Therefore, D’Angelo not only fails to disclose, but indeed teaches away from, (a) a self adhesive matrix layer containing microreservoirs of (2) diameter smaller than the thickness of the matrix layer. Proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. MPEP 2145.X.D.3, citing *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986).

Further, neither of the deficiencies discussed above are cured by Lauterbach, which does not even mention microreservoirs.

1.2 No apparent reason either in the references or the general knowledge in the art to combine and modify the references to include the missing subject matter

If the references are missing claimed features, there must be some apparent reason either in the references or the general knowledge in the art to modify the references to include the missing subject matter. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ 1385 (2007). MPEP § 2143 states that “[t]he key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been

obvious,” which should be made explicit and must be anchored by a rational underpinning, as directed by *KSR Int’l Co. v. Teleflex Inc.* This burden is not met in the present rejection based on D’Angelo in view of Lauterbach.

Applicant submits that there is no reason either in the references or the general knowledge in the art to combine and modify the cited references to arrive at instant Claim 1. Further, no reason has been articulated in the Office Action to embed microreservoirs within the self-adhesive border as opposed to a gel matrix layer as disclosed by D’Angelo. See *Id.* (an obviousness inquiry includes determining whether there was an apparent reason to combine the known elements in the fashion claimed). Even if one of skill in the art would have been motivated to make such a combination and modification (which is not admitted herein), that combination and modification would not have provided microreservoirs within a self-adhesive matrix, as required by Claim 1 for at least the following reasons:

(1) Independent components provide no reason for combination & modification:

In contrast to the present invention, D’Angelo mentions an acrylate adhesive and microcapsules as independent components of a patch. This is not sufficient to establish a *prima facie* case of obviousness. Under *KSR, supra* (emphasis added), “a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. ... [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” The present Action’s identification of a reference with microcapsules and a self-adhesive acrylate, each discussed independently in the reference, is exactly the type of hindsight reconstruction warned against in *KSR*.

(2) Combination & modification yields a patch unsatisfactory for its intended purpose: The Office Action fails to address Applicant’s argument that a modification of D’Angelo to reduce the size of the microcapsules (to have a

diameter that is less than the thickness of the layer wherein they are embedded.), far from being a routine modification as stated in the present Action (p. 9), would render the patch of D'Angelo unsatisfactory for its intended purpose. "If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." MPEP 2143.01.V, citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). If microcapsule diameter were reduced so that the microcapsules no longer adhered to the tear-off strip, the patch of D'Angelo would no longer function as intended.

- (3) **Combination & modification would change the principle of operation:** The Office Action also fails to address Applicant's argument that, alternatively, a modification of D'Angelo to reduce the size of the microcapsules would change the principle of operation of the D'Angelo patch. "If the proposed modification ... would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." MPEP 2143.01.VI, citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). If microcapsule diameter were reduced so that the microcapsules no longer adhered to the tear-off strip, the principle of operation of D'Angelo would be changed, indeed lost.
- (4) **No pattern of preferences** D'Angelo and Lauterbach (alone or in combination) clearly do not provide a pattern of preferences which point an ordinary artisan toward Claim 1. An ordinary artisan reading D'Angelo and Lauterbach, would have to choose at least:
- a. a self-adhesive matrix
 - b. a self-adhesive matrix containing microreservoirs with rotigotine free base
 - c. a self-adhesive matrix permeable to free base of rotigotine
 - d. a self-adhesive matrix substantially impermeable to protonated form of rotigotine, and
 - e. make the microreservoirs less than the thickness of the self-adhesive

matrix.

Although the Office Action dismisses Applicant's argument on p. 10 by stating: "...it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning", clearly, such a multi-step selection can only be made in hindsight with guidance from Applicant's specification to arrive at the claimed invention. It is apparent that in the instant case, "what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." In re O'Farrell, 853 F. 2d 894, 903 (Fed. Cir. 1988). "In such circumstances, where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness." In re Kubin, 561 F.3d 1351, 1359 (Fed. Cir. 2009), emphasis added.

- (5) **Generic D'Angelo disclosure:** Applicant maintains that nothing in D'Angelo would motivate one of ordinary skill to select rotigotine free base over any other pharmacological agent. In fact, the exemplary list of drugs is prefaced with the statement that "almost any drug, to some degree, can be administered transdermally" (D'Angelo, col. 1, lines 58-59).

Thus, nothing in D'Angelo, Lauterbach or the art suggests that it would be beneficial for microreservoirs to have a maximum diameter less than the thickness of the matrix layer (in D'Angelo a gel matrix layer, not a self-adhesive matrix layer) in which they are embedded.

1.3 No reasonable expectation of success

When formulating a *prima facie* case of obviousness, a reasonable expectation or predictability of success is required, as noted in MPEP § 2143.02: "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." And see *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143, 148 (C.C.P.A. 1976) (stating that there must be a

showing of a reasonable expectation of success and the alleged combination cannot be said to be “inherently” successful).

In this case, there is no basis for such predictability found in the D’Angelo and Lauterbach documents or provided based on the general knowledge in the art.

First, there is no guidance provided to make a transdermal assembly from the alleged combination having a matrix permeable to the free base of rotigotine and substantially impermeable to the protonated form of rotigotine, as found in instant Claim 1. For example, the hydrogel matrix 18 of D’Angelo likely contains enough water to produce the salt form of rotigotine; see the present specification as filed on page 6, line 24 to page 7, line 9 where it is noted that less water results in less salt form of rotigotine. Thus, the alleged transdermal assembly would have a matrix that is likely permeable to the protonated form of rotigotine, which is antithetical to Claim 1.

Second, there is also no reasonable expectation of success in making a transdermal assembly from the alleged combination where the microcapsules have a maximum diameter that is less than the thickness of the matrix. In doing so, how could the D’Angelo microcapsules remain attached to both the bottom of the tear strip 5 and to the top of the permeable membrane 13 using the microcapsule adhesive 19? Answer: They couldn’t. Note that the microcapsules still need to be attached to the tear strip 5 and permeable membrane 13 in order for the assembly to function regardless of the diameter of the microcapsules; *i.e.*, the matrix 18 layer thickness is dependent on the diameter of the microcapsules 8. There is no alternative way provided in the cited documents to replace the necessary tear off and rupture of the microcapsules in order to activate the assembly and the Office Action fails to provide an alternative means based on the general knowledge in the art and indicate how and why it would function in lieu of the tear off. Thus, a person of ordinary skill in the art would not reasonably predict that modifying the diameter of the microcapsules to be less than the matrix thickness would be successful.

As illustrated, the alleged combination of D’Angelo and Lauterbach fails to provide a reasonable expectation of success and cannot establish a *prima facie* case of obviousness.

1.4 Rejection under 35 U.S.C. §103(a): conclusion

A *prima facie* case of obviousness has not been established over the alleged combination of D'Angelo and Lauterbach at least because:

- (1) The alleged combination fails to provide for all of the elements of Claim 1.
- (2) There is no apparent reason either in the references or the general knowledge in the art to combine and modify the references to include the missing subject matter in the fashioned claimed by Applicant's Claim 1.
- (3) No reasonable expectation of success is provided by the alleged combination or the general art to recreate Applicant's Claim 1.

For any one of the reasons set forth above, a *prima facie* case of obviousness has not been established for instant Claim 1.

Notwithstanding the Examiner's remarks with respect to the subject matter of dependent Claims 2–6 and 8–13, these claims each embody all the limitations of Claim 1 from which they depend or which they reference, and are therefore nonobvious at least for the same reasons that Claim 1 is nonobvious. If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. MPEP 2143.03.

However, Applicant wishes to clarify the Examiner's statements regarding PVP and the addition of silicone adhesives, as these statements appear again to utilize the hindsight reconstruction warned against in *KSR, supra*. Specifically, the present Office Action (p. 9) alleges "that D'Angelo *et al.* teach PVP, which overlaps with the instantly claimed crystallization inhibitor." Applicant submits that the discussion of PVP in D'Angelo is focused on use of PVP as a matrix and not as a component of the microcapsules. Therefore, any combination of D'Angelo and Lauterbach (even if motivation existed for such combination, which, as shown above, is not the case) would not result in microcapsules containing PVP. Furthermore, the Action (p. 9) alleges that "it would have been obvious to a person of skill in the art to add a silicone pressure adhesive as taught by Lauterbach *et al.* to the adhesive component of the transdermal formulation for additive adhesive effect." Even if this were true, which is not admitted, addition of self-adhesive silicone to the adhesive component of the D'Angelo patch would not result in microcapsules within a self-adhesive

matrix, but simply in additional self-adhesive for the patch border to adhere the patch to the skin.

Withdrawal of the present rejection under 35 U.S.C. §103(a) is respectfully requested for at least the reasons given above.

2. Provisional obviousness-type double patenting rejections

2.1 Double patenting over Serial No. 10/429,283 in view of D'Angelo

Claims 1–6 and 8–13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 5–16 of copending application Serial No. 10/429,283, in view of D'Angelo. This rejection is provisional because the allegedly conflicting claims have not yet been patented.

The present rejection is respectfully traversed, at least for the following reason. Each of Claims 1–6 and 8–13 of the present rejection requires that the TDS self-adhesive matrix comprise a multitude of rotigotine-containing microreservoirs having a maximum diameter that is less than the thickness of the matrix. This limitation is not taught or suggested by the reference claims, nor is any disclosure found in D'Angelo that would correct this deficiency. Indeed, as shown above, it is important to D'Angelo's system that microcapsule diameter be not less than the thickness of the matrix wherein the microcapsules are embedded.

At least the distinguishing features mentioned above are therefore sufficient to create patentable distinction over Claims 5–16 of the '283 application, even in view of D'Angelo.

2.2 Double patenting over Serial No. 10/627,990 in view of D'Angelo and Lauterbach

Claims 1–6 and 8–13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 1–13 of copending application Serial No. 10/627,990, in view of D'Angelo and Lauterbach. This rejection is provisional because the allegedly conflicting claims have not yet been patented.

The present rejection is respectfully traversed, at least for the reason that the present application has an earlier filing date (22 July 2003) than the reference application (July 28, 2003), and therefore, when issued as a patent, will expire before any patent that issues from the reference application. Rejection for double patenting is warranted only where “issuance

of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent” (MPEP 804.II.B.1). That is not the case here.

Applicant notes that a terminal disclaimer was filed in the '990 application on 29 July 2008.

3. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated or rendered moot herein. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the present Action and that the Application is in condition for allowance.

If personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number below.